Rhodium Carbenoid Mediated Cyclisations. Part 2.[1] Synthesis of Cyclic Ethers[2]

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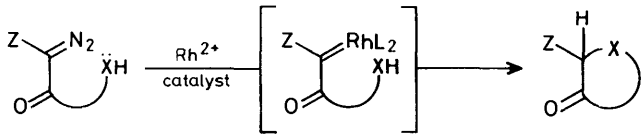
Alkylation of the dianion of methyl acetoacetate with the t-butyldimethylsilyl protected α,ω-halogeno alcohols (**1**)—(**9**) gives the β-keto esters (**1**) which are converted into the diazo alcohols (**3**) by diazo transfer and desilylation. Rhodium carbenoid cyclisation of the diazo alcohols (**3b—d**) gives the 7-membered ethers (**11**)—(**13**) in good yield. The 8-membered ether (**14**) is formed in only modest yield from the diazo alcohol (**3e**), but cyclisation of the diazo alcohol (**3f**) to the 10-membered ether (**15**) was not successful.

The thermal, photochemical, and transition metal-catalysed decomposition of α-diazocarbonyl compounds has been widely investigated,[3-5] and the intramolecular cyclisations of the resulting carbenes or carbenoids are synthetically useful reactions.[6] In recent years, effort has concentrated on the transition metal-catalysed decomposition reactions as a result of the development of new catalysts.[7-9] Rhodium(II) acetate, with its binuclear structure is a particularly effective catalyst for the decomposition of diazo compounds and since the discovery of its catalytic effect by Teyssie, Hubert, and coworkers,[10] has become the catalyst of choice for a wide range of diazo compound transformations. The rhodium(II) catalysed decomposition of diazo compounds is believed to involve a rhodium carbenoid intermediate which retains the highly electrophilic properties associated with free carbenes. Therefore, in an appropriate acyclic substrate, such an intermediate would be intercepted intramolecularly by a nucleophile to effect overall cyclisation (Scheme 1), and we have

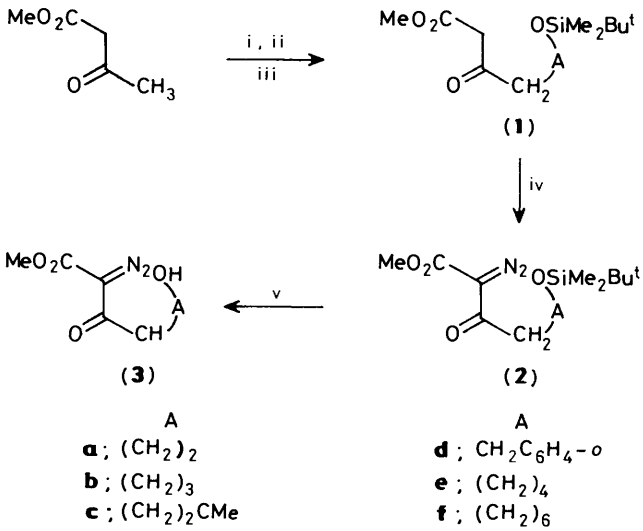


Scheme 1.

used such a reaction in the synthesis of 1,2-diazetidinones (aza-β-lactams) (Scheme 1: X = NR, Z = CO_2Et or $COCH_3$, ring size = 4).[1] We have been interested in extending this work and exploring the potential of rhodium carbenoid cyclisations as a general route to oxygen-, sulphur-, and nitrogen-containing rings (Scheme 1: X = O, S, or NR), and we now report in full the first use of this method in the synthesis of 7- and 8-membered ring ethers.[11] In parallel with our work, Rapoport's group have studied similar cyclisation reactions, and have recently published their results on the preparation of 4-, 5-, and 6-membered ring nitrogen heterocycles, and 5-membered ring ethers and thioethers.[12]

Results and Discussion

The successful carbenoid mediated cyclisation to cyclic ethers requires a formal intramolecular insertion into an O–H bond, although given the highly electrophilic nature of the rhodium carbenoid, we prefer to regard these reactions as nucleophilic attack by the alcohol OH group on the electrophile. Although intermolecular 'alkylation' of alcohols by rhodium carbenoids is known,[13] other than our own[2] and Rapoport's[12] work, the intramolecular version has not been reported. Indeed there are only isolated examples of carbenes in general reacting intramolecularly with O–H bonds, and these all lead to 5- and 6-membered rings.[14]

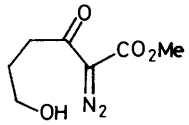
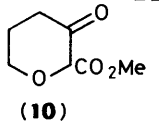
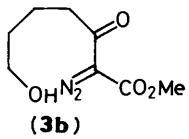
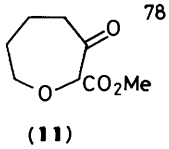
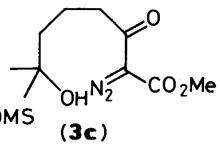
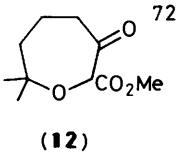
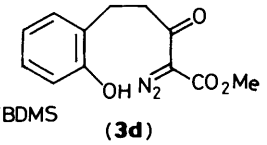
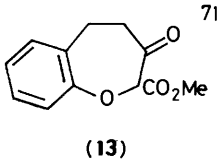
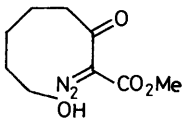
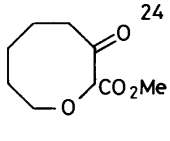
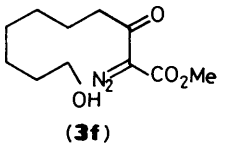
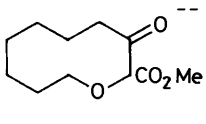


Scheme 2. *Reagents:* i, NaH, THF; ii, BuLi; iii, Hal-A-OTBDMS [(**4**)—(**9**), Table]; iv, TsN_3, Et_3N, MeCN; v, AcOH–H_2O–THF or HF–H_2O–MeCN

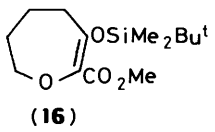
The precursors to our 7- and 8-membered cyclic ethers are the diazo alcohols (**3**), prepared in 3 steps from readily available starting materials as shown in Scheme 2. Thus methyl acetoacetate was converted into its dianion,[15] and alkylated with a t-butyldimethylsilyl (TBDMS) protected α,ω-halogeno alcohol (**4**)—(**9**) (Table) to give the β-keto esters (**1**) in reasonable yield. Diazo-transfer[16] to the β-keto esters (**1**) using tosyl azide in acetonitrile in the presence of triethylamine gave the diazo compounds (**2**) in good yield, and removal of the TBDMS group in the presence of the diazo function to give the required diazo alcohols (**3**) was achieved by the use of aqueous acetic acid or aqueous hydrofluoric acid. The diazo compounds (**2**) and (**3**), with the exception of the diazo phenol (**3d**), were yellow oils with the characteristic i.r. band at *ca.* 2 140 cm^{-1}. After column chromatography they were pure by t.l.c. and by n.m.r., although they could not be obtained analytically pure. No attempt was made to purify the diazo compounds by distillation because of the likely hazards involved. However, the diazo alcohols did not deteriorate on storage in the refrigerator.

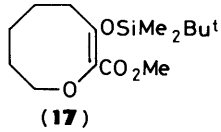
The rhodium carbenoid cyclisation reactions were carried out by adding the diazo alcohols (**3**) in benzene to a catalytic amount of rhodium(II) acetate suspended in refluxing benzene. Under these conditions the diazo alcohol (**3a**) gave a

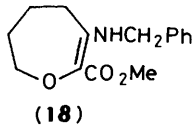
Table. Preparation and cyclisation of the diazo alcohols (**9**)

Hal-A-OTBDMS	Diazo compound	Cyclic ether	Yield (%)
$I(CH_2)_2OTBDMS$ (**4**)	 (**3a**)	 (**10**)	--
$I(CH_2)_3OTBDMS$ (**5**)	 (**3b**)	 (**11**)	78
$I(CH_2)_2CMe_2OTBDMS$ (**6**)	 (**3c**)	 (**12**)	72
$BrCH_2C_6H_4OTBDMS$ (**7**)	 (**3d**)	 (**13**)	71
$I(CH_2)_4OTBDMS$ (**8**)	 (**3e**)	 (**14**)	24
$I(CH_2)_6OTBDMS$ (**9**)	 (**3f**)	 (**15**)	--

surprisingly complex mixture, which did not appear to contain the expected six-membered ring (**10**). In contrast, however, the diazo alcohol (**3b**) cyclised smoothly in the presence of rhodium(II) acetate to give the 3-oxo-oxepane ester (**11**) in good yield (78%). The cyclisation reaction is not subjected to steric hindrance at the oxygen centre, the tertiary alcohol (**3c**) cyclising just as easily in 72% yield. Similarly the diazo phenol (**3d**) readily cyclised to give the 3-oxotetrahydrobenzoxepine (**13**) (71%). As expected, cyclisation of the diazo alcohol (**3e**) proceeded less readily, and the 8-membered cyclic ether (**14**) was isolated in only 24% yield. Nevertheless, the formation of the oxecane (**14**) under these conditions is noteworthy since 8-membered rings are among the most difficult form by any ring closure method.[17] However, cyclisation of the diazo alcohol (**3f**) to the 10-membered ether (**15**) was not successful. Instead, a complex mixture of products resulted, although there was some evidence for cyclopentanone formation by competing C–H insertion.[18]


(**16**)


(**17**)


(**18**)

The structures of the cyclised products were supported by their spectral properties, although their n.m.r. spectra (both ^1H and ^{13}C) were complicated by the presence of both keto and enol tautomers of the cyclic β-keto ester group. As an additional structure proof, the oxepane (**11**) and the oxecane (**14**) were converted into their TBDMS enol derivatives (**16**) and (**17**) by reaction with TBDMS trifluoromethanesulphonate in the presence of triethylamine. The n.m.r. spectra of the enol ethers (**16**) and (**17**) were much simpler and easier to assign. The 3-oxo-oxepane (**11**) also reacted with benzylamine to give the crystalline enamine (**18**), the structure of which was confirmed by *X*-ray crystallography.[2]

Thus the rhodium carbenoid mediated cyclisations to 7-membered ring ethers occur easily in good yield. Although O–H bonds are thermodynamically stronger than C–H bonds, competing C–H insertion reactions are not a problem in these cases, suggesting that the cyclisation proceeds by nucleophilic attack by the OH group on the rhodium carbenoid intermediate rather than by a true insertion mechanism. In the case of 8-membered ring formation, the yield is much lower, and with larger rings still, C–H insertion reactions appear to supervene.

Experimental

I.r. spectra were recorded as thin films or as solutions in chloroform on Perkin-Elmer 298 or 1 710 spectrophotometers, and calibrated against polystyrene. ^1H N.m.r. were recorded on a Bruker WM250 (operating at 250 MHz), on a Perkin-Elmer R32 (operating at 90 MHz), or on a Varian EM360 spectrometer (operating at 60 MHz). ^{13}C N.m.r. spectra were recorded on a Bruker instrument at 62.9 MHz. Mass spectra were recorded on a VG Micromass 7070B mass spectrometer operating at 70 eV using a direct insertion probe. Silica gel (Merck type 60H) was used for column chromatography. Ether refers to diethyl ether and light petroleum refers to that fraction with b.p. 40—60 °C. Tetrahydrofuran (THF) and ether were dried with potassium and sodium respectively, using the benzophenone ketyl radical as indicator. Other solvents were dried by standard procedures. Distillations of products were carried out in a Kugelrohr apparatus.

General Procedure for the Preparation of t-Butyldimethylsiloxyiodoalkanes.—A stirred solution of the chloro alcohol in dimethylformamide (2 ml/g alcohol) was treated with t-butyldimethylsilyl chloride (1.2 equiv.) and imidazole (2.5 equiv.) under nitrogen at room temperature. The reaction mixture was stirred 1—3 days, poured into water, and extracted with light petroleum. The organic phase was washed with hydrochloric acid (10%), and with water until neutral, dried ($MgSO_4$), and evaporated. The residue was distilled to give the t-butyldimethylsiloxychloroalkane.

The above chloride was dissolved in acetone (1 ml/0.55 mmol chloride) and treated with sodium iodide (2.2 equiv.). The solution was heated under reflux under nitrogen for 3 days. The

precipitate was filtered off and washed with dichloromethane. The combined filtrate and washings were diluted with dichloromethane, washed with water, aqueous sodium sulphite (10%), and brine, dried ($MgSO_4$), and evaporated to give the t-butyldimethylsiloxyiodoalkane as a colourless oil. The following compounds were thus prepared.

1-(*t-Butyldimethylsiloxy*)-2-*iodoethane* (**4**). δ_H(90 MHz; $CDCl_3$) 0.10 (6 H, s, Me_2Si), 0.90 (9 H, s, Bu^{t}Si), 3.20 (2 H, t, *J* 7.0 Hz, CH_2I), and 3.85 (3 H, t, *J* 7.0 Hz, CH_2O).

1-(*t-Butyldimethylsiloxy*)-3-*iodopropane* (**5**). B.p. 100 °C at 10 mmHg (Found: C, 35.9; H, 7.25. $C_9H_{21}IOSi$ requires C, 36.0; H, 7.05%); $\nu_{max.}$(film) 2 960, 2 920, 2 890, 2 860, 1 470, 1 425, 1 380, 1 360, 1 255. 1 180, 1 130, 1 100, 1 050, 1 000, 830, 775, 720, and 670 cm^{-1}; δ_H(90 MHz; $CDCl_3$) 0.15 (6 H, s, Me_2Si), 0.95 (9 H, s, Bu^{t}Si), 2.05 (2 H, quint., $CH_2CH_2CH_2$), 3.30 (2 H, t, *J* 6.5 Hz, CH_2I), and 3.70 (2 H, t, *J* 6.5 Hz, CH_2O); *m/z* 243 ($M^+ - C_4H_9$), 215, 185, 147, and 115.

1-(*t-Butyldimethylsiloxy*)-6-*iodohexane* (**9**). B.p. 100 °C at 0.01 mmHg (Found: C, 42.4; H, 8.2; I, 36.9. $C_{21}H_{27}IOSi$ requires C, 42.10; H, 7.95; I, 37.1%); $\nu_{max.}$(film) 2 960, 2 940, 2 900, 2 860, 1 470, 1 460, 1 390, 1 360, 1 260, 1 200, 1 100, 1 010, 835, 780, and 660 cm^{-1}; δ_H(90 MHz; $CDCl_3$) 0.15 (6 H, s, Me_2Si), 1.00 (9 H, s, Bu^{t}Si), 1.35—2.15 [8 H, m, $ICH_2(CH_2)_4CH_2$], 3.30 (2 H, t, *J* 7.0 Hz, CH_2I), and 3.75 (2 H, t, *J* 6.0 Hz, CH_2O); *m/z* 285 ($M^+ - C_4H_9$), 215, 185, and 83.

1-(*t-Butyldimethylsiloxy*)-4-*iodobutane* (**8**).—A solution of freshly distilled THF (2 ml, 1.772 g, 24.61 mmol) in dry acetonitrile (15 ml), was treated with t-butyldimethylsilyl chloride (4.08 g, 27.07 mmol) followed by sodium iodide (4.06 g, 27.07 mmol). The reaction mixture was stirred at room temperature under nitrogen for 21 h. The resulting orange suspension was poured into water (50 ml), extracted with ether (50 ml), and the extract washed with aqueous sodium sulphite (10%; 30 ml) and water (2 × 25 ml) until neutral, dried ($MgSO_4$), and evaporated. The crude product (7.24 g) was chromatographed on silica (ether–light petroleum) to give the title compound (**8**) as a colourless oil (5.63 g, 73%), b.p. 125—135 °C at 0.3 mmHg; $\nu_{max.}$(film), 2 960, 2 940, 2 900, 2 860, 1 470, 1 460, 1 390, 1 260, 1 230, 1 100, 960, 840, 780, and 610 cm^{-1}; δ_H(250 MHz; $CDCl_3$), 0.03 (6 H, s, Me_2Si), 0.80 (9 H, s, Bu^{t}Si), 1.59 (2 H, quint., *J* 6.5 Hz, $CH_2CH_2CH_2I$), 1.89 (2 H, quint., *J* 6.5 Hz, CH_2CH_2I), 3.20 (2 H, t, *J* 6.5 Hz, CH_2I), and 3.61 (2 H, t, *J* 6.5 Hz, CH_2O); *m/z* 299 ($M^+ - CH_3$), 257, 215, 185, and 129.

2-(*t-Butyldimethylsiloxy*)-4-*iodo*-2-*methylbutane* (**6**).—4-Bromo-2-methylbutan-2-ol was prepared (65%) by addition of methyl magnesium iodide to methyl 3-bromopropionate following a literature procedure.[19] 2,6-Dimethylpyridine (3.65 ml, 3.378 g, 31.52 mmol) was treated at 0 °C under nitrogen with t-butyldimethylsilyl trifluoromethanesulphonate (4.43 ml, 5 g, 18.91 mmol). The reaction mixture was stirred for 0.5 h before addition of a solution of 4-bromo-2-methylbutan-2-ol (2.106 g, 12.61 mmol) in dry dichloromethane (3 ml). The mixture was stirred for a further 2.75 h with warming to room temperature, poured into a mixture of ice–water (50 ml) and saturated aqueous sodium hydrogen carbonate (50 ml), and extracted with dichloromethane (2 × 50 ml). The combined extracts were washed with water (2 × 50 ml), dried ($MgSO_4$), and evaporated to give a yellow oil. The crude product (7.60 g) was chromatographed on silica (ether–light petroleum) to give 2-1-*bromo*-(*t-butyldimethylsiloxy*)-3-*methylbutane* (3.012 g, 85%), b.p. 150 °C at 1.5 mmHg (Found: C, 47.2; H, 9.2; Br, 28.5. $C_{11}H_{25}BrOSi$ requires C, 47.0; H, 9.0; Br, 28.4%); $\nu_{max.}$(film) 2 960, 2 940, 2 900, 2 860, 1 480, 1 470, 1 370, 1 260, 1 210, 1 050, 940, 840, 780, and 700 cm^{-1}; δ_H(90 MHz; $CDCl_3$) 0.15 (6 H, s, Me_2Si), 0.90 (9 H, s, Bu^{t}Si), 1.30 (6 H, s, Me_2C), 2.10 (2 H, ~t, *J* 8.0 Hz, CH_2CH_2Br), and 3.50 (2 H, ~t, *J* 8.0 Hz, CH_2Br); *m/z* 265/267 ($M^+ - CH_3$) and 223/225 ($M^+ - C_4H_9$).

The above bromide (2.28 g) was treated with sodium iodide according to the general method to give the *title compound* (**6**) (2.05 g, 77%), b.p. 90—100 °C at 0.35 mmHg (Found: M^+, 271.0011. $C_{11}H_{25}IOSi - C_4H_9$ requires 271.0015); $\nu_{max.}$(film) 2 960, 2 940, 1 470, 1 460, 1 380, 1 365, 1 260, 1 190, 1 100, 1 040, 950, 840, 775, and 690 cm^{-1}; δ_H(90 MHz; $CDCl_3$), 0.10 (6 H, s, Me_2Si), 0.90 (9 H, s, Bu^{t}Si), 1.25 (6 H, s, Me_2C), 2.10 (2 H, ~t, *J* 8.0 Hz, CH_2CH_2I), and 3.25 (2 H, ~t, *J*, 8.0 Hz, CH_2I); *m/z* 313 ($M^+ - CH_3$), 271. 243, 185, 173, and 75.

2-(*t-Butyldimethylsiloxy*)*benzyl Bromide* (**1**).—Reaction of salicaldehyde with t-butyldimethylsilyl chloride as described above gave 2-(t-butyldimethylsiloxy)benzaldehyde, b.p. 115 °C at 0.05 mmHg (Found: C, 66.0; H, 8.8. $C_{13}H_{20}O_2Si$ requires C, 66.05; H, 8.5%); $\nu_{max.}$(film) 2 960, 2 940, 2 900, 2 870, 1 690, 1 600, 1 480, 1 460, 1 390, 1 310, 1 280, 1 260, 1 160, 920, 845, 830, and 635 cm^{-1}; δ_H(90 MHz; $CDCl_3$) 0.25 (6 H, s, Me_2Si), 1.00 (9 H, s, Bu^{t}Si), 6.85—7.10 (2 H, m, ArH), 7.45 (1 H, m, ArH), 7.80 (1 H, m, ArH), and 10.45 (1 H, s, *CH*O); *m/z* 237 (MH^+), 221, 195, 179, and 75.

A solution of the above aldehyde (7.87 g, 33.34 mmol) in methanol (100 ml) was treated with sodium borohydride (1.577 g, 41.68 mmol). The reaction mixture was stirred at room temperature under nitrogen for 6 h. The solution was treated with brine (70 ml), concentrated, and extracted with ether (2 × 50 ml). The ether extracts were washed with aqueous hydrochloric acid (10%) and water (2 × 100 ml), dried ($MgSO_4$), and evaporated to give 2-(*t-butyldimethylsiloxy*)-*benzyl alcohol* (7.261 g, 92%) as an oil which crystallised with time, b.p. 115 °C at 0.03 mmHg, m.p. 28—30 °C (Found: C, 65.45; H, 9.4. $C_{13}H_{22}O_2Si$ requires C, 65.5; H, 9.3%); $\nu_{max.}$(film) 3 350, 2 960, 2 940, 2 900, 2 860, 1 600, 1 585, 1 490, 1 455, 1 260, 1 040, 920, 780, and 665 cm^{-1}; δ_H(90 MHz; $CDCl_3$) 0.30 (6 H, s, Me_2Si), 1.00 (9 H, s, Bu^{t}Si), 2.15 (1 H, br s, CH_2OH), 4.70 (2 H, br s, CH_2OH), and 6.75—7.40 (4 H, m, ArH); *m/z* 238 (M^+), 221, 181, 163, and 75.

A solution of the above alcohol (7.00 g, 29.41 mmol) in acetonitrile (140 ml) was treated with carbon tetrabromide (10.24 g, 30.88 mmol) followed by triphenylphosphine (8.10 g, 30.88 mmol) at 0 °C under nitrogen. The reaction mixture was stirred at room temperature for 20 h and concentrated. The resulting orange residue was chromatographed on silica (ether–light petroleum) to give the *title compound* (**7**) as a colourless oil (7.62 g, 86%), b.p. ~130 °C at 0.08 mmHg (Found: C, 51.8; H, 7.0; Br, 26.3. $C_{13}H_{21}BrOSi$ requires C, 51.8; H, 7.0; Br, 26.5%); $\nu_{max.}$(film) 2 960, 2 940, 2 900, 2 860, 1 600, 1 585, 1 490, 1 455, 1 390, 1 270, 1 040, 920, 780, and 610 cm^{-1}; δ_H(90 MHz; $CDCl_3$) 0.30 (6 H, s, Me_2Si), 1.05 (9 H, s, Bu^{t}Si), 4.55 (2 H, s, CH_2Br), and 6.70—7.40 (4 H, m, ArH); *m/z* 300/302 (M^+), 285/287, 243/245, and 221.

Dianion Reactions

Methyl 6-(*t-Butyldimethylsiloxy*)-3-*oxohexanoate* (**1a**).—A suspension of sodium hydride (40% dispersion in oil; 1.29 g, 21.49 mmol) in THF (50 ml) was prepared under nitrogen at 0 °C. Methyl acetoacetate (2.10 ml, 2.27 g, 9.54 mmol) was added, and the mixture was stirred for 0.25 h. Butyl-lithium (1.6M; 12.74 ml, 1.30 h, 20.38 mmol) was added, followed after a further 0.25 h by a solution of 2-(t-butyldimethylsiloxy)-1-iodoethane (**4**) (5.83 g, 20.38 mmol) in THF (4 ml). The mixture was stirred for 2 h at 0 °C, and the dark orange suspension was poured into water (100 ml). The mixture was made slightly acidic, and extracted with ether (100 ml). The organic phase was washed with water (4 × 50 ml), dried ($MgSO_4$), and evaporated to give an orange oil (6.94 g). Chromatography on silica (ether–light petroleum) gave the *title compound* (**1a**) as a pale yellow oil (3.51 g, 66%), b.p. 70—72 °C at 0.35 mmHg (Found: C, 56.7; H,

9.5. $C_{13}H_{26}O_4Si$ requires C, 56.9; H, 9.55%); $\nu_{max.}$(film) 2 960, 2 930, 2 885, 2 866, 1 750, 1 720, 1 655, 1 630, 1 435, 1 255, 1 100, 840, and 780 cm^{-1}; δ_H(90 MHz; $CDCl_3$) 0.10 (6 H, s, Me_2Si), 0.90 (9 H, s, Bu^{t}Si), 1.85 (2 H, quint., *J* 6.5 Hz, $CH_2CH_2CH_2$), 2.70 (2 H, t, *J* 6.5 Hz, CH_2CO), 3.50 (2 H, s, $COCH_2CO$), 3.70 (2 H, t, *J* 6.5 Hz, CH_2O), and 3.80 (3 H, s, OCH_3); *m/z* 259 ($M^+ - CH_3$), 243, 217, 185, 175, 157, and 75.

Methyl 7-(t-Butyldimethylsiloxy)-3-oxoheptanoate (**1b**).—The dianion of methyl acetoacetate (2.30 ml, 2.47 g, 21.3 mmol), prepared by reaction with sodium hydride (40%; 1.40 g, 23.4 mmol) and butyl-lithium (1.6M; 13.88 ml, 1.42 g, 22.2 mmol) in dry THF (53 ml), was treated with a solution of 1-(t-butyldimethylsiloxy)-3-iodopropane (**5**) (6.66 g, 22.2 mmol) in dry THF (4 ml) as described above. Work-up and chromatography gave the *title compound* (**1b**) as a colourless oil (4.12 g, 67%), b.p. ~75 °C/0.45 mmHg (Found: C, 58.0; H, 9.45. $C_{14}H_{28}O_4Si$ requires C, 58.3; H, 9.8%); $\nu_{max.}$(film) 2 980, 2 920, 2 890, 2 860, 1 750, 1 720, 1 650, 1 630, 1 435, 1 400, 1 360, 1 320, 1 255, 1 150, 1 100, 1 000, 835, and 775 cm^{-1}; δ_H(90 MHz; $CDCl_3$) 0.10 (6 H, s, Me_2Si), 0.90 (9 H, s, Bu^{t}Si), 1.45—1.75 (4 H, m, $CH_2CH_2CH_2OSi$), 2.50 (2 H, t, *J* 7.0 Hz, CH_2CO), 3.45 (2 H, s, $COCH_2CO$), 3.60 (2 H, t, *J* 6.5 Hz, CH_2OSi), and 3.70 (3 H, s, OCH_3); *m/z* 273 ($M^+ - CH_3$, 257, 231, 199, and 99.

Methyl 7-(t-Butyldimethylsiloxy)-7,7-dimethyl-3-oxoheptanoate (**1c**).—The dianion of methyl acetoacetate (0.62 ml, 667 mg, 5.75 mmol), prepared by reaction with sodium hydride (50%; 298 mg, 6.21 mmol) and butyl-lithium (1.6M; 3.68 ml, 377 mg, 5.89 mmol) in dry THF (14 ml), was treated with a solution of 2-(t-butyldimethylsiloxy)-4-iodo-2-methylbutane (**6**) (1.933 g, 5.89 mmol) in dry THF (2 ml) as described above. Work-up and chromatography gave recovered iodide (**6**) (651 mg, 46%) and the *title compound* (**1c**) as a colourless oil (527 mg, 29%), b.p. 130 °C at 0.20 mmHg (Found: M^+, 301.1844. $C_{16}H_{32}O_4Si - CH_3$ requires 301.1835); $\nu_{max.}$(film) 2 960, 2 940, 2 900, 2 870, 1 750, 1 720, 1 650, 1 625, 1 440, 1 410, 1 260, 830, and 770 cm^{-1}; δ_H(90 MHz; $CDCl_3$) 0.10 (6 H, s, Me_2Si), 0.85 (9 H, s, Bu^{t}Si), 1.10—1.85 (4 H, m, $COCH_2CH_2CH_2$), 1.20 [6 H, s, $CH_2C(CH_3)_2$], 2.55 (2 H, t, *J* 7.0 Hz, $COCH_2$), 3.40 (2 H, s, $COCH_2CO$), and 3.70 (3 H, s, OCH_3); *m/z* 301 ($M^+ - CH_3$), 259, 203, 173, and 75.

Methyl 5-(2-t-Butyldimethylsiloxyphenyl)-3-oxopentanoate (**1d**).—The dianion of methyl acetoacetate (0.68 ml, 732 mg, 6.4 mmol), prepared by reaction with sodium hydride (50%; 310 mg, 6.75 mmol) and butyl-lithium (1.6M; 4 ml, 409 mg, 6.4 mmol) in dry THF (15 ml), was treated with a solution of 2-(t-butyldimethylsiloxy)benzyl bromide (**7**) (1.926 g, 6.4 mmol) in dry THF (2 ml) as described above. Work-up and chromatography gave the *title compound* (**1d**) as a yellow oil (1.698 g, 50%), b.p. 103 °C/0.10 mmHg (Found: C, 63.95; H, 8.5. $C_{18}H_{28}O_4Si$ requires C, 64.25; H, 8.4%); $\nu_{max.}$(film) 2 960, 2 940, 2 900, 2 860, 1 750, 1 720, 1 625, 1 600, 1 580, 1 490, 1 250, 920, 835, and 750 cm^{-1}; δ_H(90 MHz; $CDCl_3$) 0.25 (6 H, s, Me_2Si), 1.00 (9 H, s, Bu^{t}Si), 2.85 (4 H, br s, CH_2CH_2CO), 3.40 (2 H, s, $COCH_2CO$), 3.70 (3 H, s, OCH_3), and 6.70—7.25 (4 H, m, ArH); *m/z* 321 ($M^+ - CH_3$), 305, 279, and 173.

Methyl 8-(t-Butyldimethylsiloxy)-3-oxo-octanoate (**1e**).—The dianion of methyl acetoacetate (1.32 ml, 1.417 g, 12.22 mmol), prepared by reaction with sodium hydride (50; 0.645 g, 13.44 mmol) and butyl-lithium (1.6M; 8.0 ml, 0.815 g, 12.74 mmol) in dry THF (30 ml), was treated with a solution of 4-(t-butyldimethylsiloxy)-1-iodobutane (**8**) (4.00 g, 12.74 mmol) in dry THF (2.5 ml) as described above. Work-up and chromatography gave the *title compound* (**1e**) as a pale yellow oil (2.723 g, 74%), b.p. 150 °C at 0.20 mmHg (Found: C, 59.7; H, 10.3. $C_{15}H_{30}O_4Si$ requires C, 59.6; H, 10.0%); $\nu_{max.}$(film) 2 960, 2 940, 2 900, 2 865, 1 750, 1 720, 1 630, 1 440, 1 320, 1 260, 1 100, 840, and 780 cm^{-1}; δ_H(90 MHz; $CDCl_3$) 0.05 (6 H, s, Me_2Si), 0.90 (9 H, s, Bu^{t}Si), 1.20—1.85 [6 H, m, $(CH_2)_3CH_2O$], 2.55 (2 H, t, *J* 6.0 Hz, CH_2CO), 3.40 (2 H, s, $COCH_2CO$), 3.60 (2 H, t, *J* 6.0 Hz, CH_2O), and 3.70 (3 H, s, OCH_3); *m/z* 287 ($M^+ - CH_3$), 271, 245, 171, and 75.

Methyl 10-(t-Butyldimethylsiloxy)-3-oxodecanoate (**1f**).—The dianion of methyl acetoacetate (0.60 ml, 651 mg, 5.61 mmol), prepared by reaction with sodium hydride (50%; 296 mg, 6.17 mmol) and butyl-lithium (1.6M; 3.65 ml, 375 mg, 5.85 mmol) in dry THF (14 ml), was treated with a solution of 1-(t-butyldimethylsiloxy)-6-iodohexane (**9**) (2.00 g, 5.85 mmol) in dry THF (2 ml) as described above. Work-up and chromatography gave the *title compound* (**1f**) as a colourless oil (1.42 g, 74%), b.p. ~150 °C/0.02 mmHg (Found: M^+, 331.2314. $C_{17}H_{34}O_4Si + H$ requires 331.2305); $\nu_{max.}$(film) 2 960, 2 940, 2 860, 1 750, 1 720, 1 650, 1 630, 1 460, 1 440, 1 320, 1 250, 1 100, 835, 775, and 660 cm^{-1}; δ_H(90 MHz; $CDCl_3$) 0.5 (6 H, s, Me_2Si), 0.90 (9 H, s, Bu^{t}Si), 1.05—1.80 [10 H, m, $(CH_2)_5CH_2O$], 2.50 (2 H, t, *J* 7.0 Hz, CH_2CO), 3.40 (2 H, s, $COCH_2CO$), 3.60 (2 H, t, *J* 6.0 Hz, CH_2O), and 3.70 (3 H, s, OCH_3); *m/z* 331 (MH^+), 315, 299, 285, 273, and 75.

Preparation of Diazo Compounds

Methyl 6-(t-Butyldimethylsiloxy)-2-diazo-3-oxohexanoate (**2a**).—A solution of methyl 6-(t-butyldimethylsiloxy)-3-oxohexanoate (**1a**) (3.00 g, 10.95 mmol) and tosyl azide (4.14 g, 21.02 mmol) in dry acetonitrile (69 ml) was treated with dropwise at 0 °C under nitrogen with triethylamine (1.90 ml, 1.38 g, 13.63 mmol). After 5.5 h, the solution was carefully evaporated to give a yellow solid which was dissolved in ether (150 ml), and the solution washed with water (200 ml) aqueous sodium hydroxide (5%; 50 ml), and then water (4 × 50 ml) until neutral, dried ($MgSO_4$), and evaporated to give a yellow oil (4.76 g) which was chromatographed on silica (dichloromethane) to give the *title compound* (**2a**) as a yellow oil (2.89 g, 89%); $\nu_{max.}$(film), 2 960, 2 930, 2 900, 2 860, 2 140, 1 730, 1 660, 1 440, 1 305, 1 260, 1 210, 1 100, 1 020, 960, 840, 780, and 745 cm^{-1}; δ_H(90 MHz; $CDCl_3$) 0.05 (6 H, s, Me_2Si), 0.90 (9 H, s, Bu^{t}Si), 1.85 (2 H, quint., *J* 7.5 Hz, $CH_2CH_2CH_2$), 2.90 (2 H, t, *J* 7.0 Hz, CH_2CO), 1.65 (2 H, t, *J* 7.0 Hz, CH_2O), and 3.85 (3 H, s, OCH_3); *m/z* 285 ($M^+ - CH_3$), 272, 269, 257, 243, 215, and 89.

Methyl 7-(t-Butyldimethylsiloxy)-2-diazo-3-oxoheptanoate (**2b**).—A solution of methyl 7-(t-butyldimethylsiloxy)-3-oxoheptanoate (**1b**) (436 mg, 1.51 mmol) and tosyl azide (571 mg, 2.90 mmol) in dry acetonitrile (9.5 ml) was treated with triethylamine (0.26 ml, 190 mg, 1.88 mmol) dropwise at 0 °C as described above. Similar work-up and chromatography gave the *title compound* (**2b**) as a pale yellow oil (426 mg, 90%); $\nu_{max.}$(film) 2 960, 2 935, 2 860, 2 140, 1 725, 1 660, 1 435, 1 310, 1 255, 1 210, 1 100, 1 000, 840, 780, and 745 cm^{-1}; δ_H(90 MHz; $CDCl_3$) 0.10 (6 H, s, Me_2Si), 0.90 (9 H, s, Bu^{t}Si), 1.55—1.90 (4 H, m, $CH_2CH_2CH_2O$), 2.90 (2 H, t, *J* 6.5 Hz, CH_2CO), 3.65 (2 H, t, *J* 6.5 Hz, CH_2OSi), and 3.85 (3 H, s, OCH_3); *m/z* 257 ($M^+ - C_4H_9$), 229 and 89.

Methyl 7-(t-Butyldimethylsiloxy)-2-diazo-7,7-dimethyl-3-oxoheptanoate (**2c**).—A solution of methyl 7-(t-butyldimethylsiloxy)-7,7-dimethyl-3-oxoheptanoate (**1c**) (478 mg, 1.51 mmol) and tosyl azide (565 mg, 2.87 mmol) in dry acetonitrile (10 ml) was treated with triethylamine (0.26 ml, 189 mg, 1.88 mmol) dropwise at 0 °C as described above. Similar work-up and chromatography gave the *title compound* (**2c**) as a yellow oil (394 mg, 76%); $\nu_{max.}$(film) 2 960, 2 940, 2 900, 2 860, 2 140, 1 725, 1 665, 1 460, 1 440, 1 365, 1 310, 1 255, 1 040, 840, 775, and 690

cm^{-1}; δ_H(90 MHz; $CDCl_3$) 0.05 (6 H, s, Me_2Si), 0.80 (9 H, s, Bu^{t}Si), 1.15—1.90 (4 H, m, $COCH_2CH_2CH_2$), 1.20 [6 H, s, $CH_2C(CH_3)_2$], 2.80 (2 H, 5, *J* 7.0 Hz, CH_2CO), and 3.80 (3 H, s, OCH_3); *m/z* 327 ($M^+ - CH_3$), 285, 257, 89, and 75.

Methyl 5-(2-*t-Butyldimethylsiloxyphenyl*)-2-*diazo*-3-*oxopentanoate* (**2d**).—A solution of methyl 5-(2-t-butyldimethylsiloxyphenyl)-3-oxopentanoate (**1d**) (2.607 g, 7.76 mmol) and tosyl azide (1.605 g, 8.15 mmol) in dry acetonitrile (52 ml) was treated with triethylamine (1.34 ml, 972 mg, 9.62 mmol) at 0 °C under nitrogen as described above. Similar work-up and chromatography gave the *title compound* (**2d**) as a dark orange oil (2.761 g, 98%); $\nu_{max.}$(film) 2 960, 2 940, 2 900, 2 865, 2 140, 1 720, 1 650, 1 600, 1 580, 1 490, 1 130, 1 100, 920, 840, and 660 cm^{-1}; δ_H(90 MHz; $CDCl_3$) 0.25 (6 H, s, Me_2Si), 1.00 (9 H, s, Bu^{t}Si), 2.85—3.30 (4 H, m, CH_2CH_2CO), 3.80 (3 H, s, OCH_3), and 6.75—7.30 (4 H, m, ArH); *m/z* 347 ($M^+ - CH_3$), 305, 277, and 91.

Methyl 8-(t-*Butyldimethylsiloxy*)-2-*diazo*-3-*oxo-octanoate* (**2e**).—A solution of methyl 8-(t-butyldimethylsiloxy)-3-oxo-octanoate (**1e**) (2.615 g, 8.66 mmol) and tosyl azide (3.241 g, 16.45 mmol) in dry acetonitrile (55 ml) was treated with triethylamine (1.50 ml, 1.087 g, 10.76 mmol) dropwise at 0 °C under nitrogen as described above. Similar work-up and chromatography gave the *title compound* (**2e**) as a yellow oil (2.50 g, 88%); $\nu_{max.}$(film) 2 960, 2 940, 2 880, 2 140, 1 720, 1 655, 1 440, 1 320, 1 130, 1 040, 920, and 740 cm^{-1}; δ_H(90 MHz; $CDCl_3$) 0.10 (6 H, s, Me_2Si), 0.90 (9 H, s, Bu^{t}Si), 1.20—1.90 [6 H, m, $(CH_2)_3CH_2O$], 2.85 (2 H, t, *J* 7.0 Hz, CH_2CO), 3.60 (2 H, t, *J* 6.0 Hz, CH_2O), and 3.80 (3 H, s, OCH_3); *m/z* 328 (M^+), 313, 297, 285, 271, 343, 89, and 75.

Methyl 10-(*t-Butyldimethylsiloxy*)-2-*diazo*-3-*oxodecanoate* (**2f**).—A solution of methyl 10-(t-butyldimethylsiloxy)-3-oxo-decanoate (**1f**) (1.210 g, 3.67 mmol) and tosyl azide (1.374 g, 6.97 mmol) in dry acetonitrile (24 ml) was treated with triethylamine (0.69 ml, 498 mg, 4.93 mmol) dropwise at 0 °C under nitrogen as described above. Similar work-up and chromatography gave the *title compound* (**2f**) as yellow oil (1.258 g, 96%); $\nu_{max.}$(film) 2 960, 2 940, 2 860, 2 140, 1 725, 1 660, 1 460, 1 440, 1 310, 1 215, 1 100, 840, 780, and 740 cm^{-1}; δ_H(90 MHz; $CDCl_3$) 0.00 (6 H, s, Me_2Si), 0.85 (9 H, s, Bu^{t}Si), 1.10—1.80 [10 H, m, $(CH_2)_5CH_2O$], 2.80 (2 H, t, *J* 7.0 Hz, CH_2CO), 3.55 (2 H, t, *J* 7.0 Hz, CH_2O), and 3.80 (3 H, s, OCH_3); *m/z* 356 (M^+), 271, 239, 89, and 75.

Preparation of Diazo Alcohols

Methyl 2-*Diazo*-6-*hydroxy*-3-*oxohexanoate* (**3a**).—A solution of methyl 6-(t-butyldimethylsiloxy)-2-diazo-3-oxohexanoate (**2a**) (2.50 g, 8.33 mmol) in THF (8 ml) was treated with a solution of glacial acetic acid (24 ml) and water (8 ml). The reaction mixture was stirred at room temperature for 5 h, evaporated, poured into water (100 ml), and extracted with dichloromethane (3 × 50 ml). The combined extracts were washed with saturated aqueous sodium hydrogen carbonate (5 × 100 ml) and water (2 × 50 ml), dried ($MgSO_4$), and evaporated to give a yellow oil (2.05 g). The crude product was chromatographed on silica (light petroleum–ether) to give the *title compound* (**3a**) as a pale yellow oil (1.14 g, 74%); $\nu_{max.}$(film) 3 425, 2 960, 2 860, 2 140, 1 725, 1 660, 1 440, 1 310, 1 210, 1 130, 1 020, and 745 cm^{-1}; δ_H(90 MHz; $CDCl_3$) 1.90 (2 H, quint., *J* 7.0 Hz, $CH_2CH_2CH_2$), 2.30—2.50 (1 H, br s, CH_2OH), 3.00 (2 H, t, *J* 7.0 Hz, CH_2CO), 3.70 (2 H, t, *J* 7.0 Hz, CH_2OH), and 3.85 (3 H, s, LCH_3); *m/z* 187 (MH^+), 157 and 142.

Methyl 2-*Diazo*-7-*hydroxy*-3-*oxoheptanoate* (**3b**).—A solution of methyl 7-(t-butyldimethylsiloxy)-2-diazo-3-oxoheptanoate (**2b**) (3.65 g, 11.62 mmol) in THF (8 ml) was treated with glacial acetic acid (24 ml) and water (8 ml). The reaction mixture was stirred at room temperature as described above. Similar work-up and chromatography gave the *title compound* (**3b**) as a yellow oil (1.484 g, 64%); $\nu_{max.}$(film) 3 400, 2 960, 2 860, 2 140, 1 745, 1 660, 1 440, 1 310, and 870 cm^{-1}; δ_H(250 MHz; $CDCl_3$) 1.46—1.71 (4 H, m, $CH_2CH_2CH_2OH$), 2.78 (2 H, t, *J* 7.3 Hz, CH_2CO), 3.54 (2 H, t, *J* 6.25 Hz, CH_2OH), 3.75 (3 H, s, OCH_3), and 5.83 (1 H, s, *OH*); *m/z* 182 ($M^+ - N_2$).

Methyl 2-*Diazo*-7-*hydroxy*-7,7-*dimethyl*-3-*oxoheptanoate* (**3c**).—A solution of methyl 7-(t-butyldimethylsiloxy)-2-diazo-7,7-dimethyl-3-oxoheptanoate (**2c**) (172 mg, 0.503 mmol) in THF (0.8 ml) was treated with glacial acetic acid (2.4 ml) and water (0.8 ml). The reaction mixture was heated to 40 °C, stirred for 0.5 h, and worked up as described above. Chromatography gave the *title compound* (**3c**) as a yellow oil (71 mg, 62%); $\nu_{max.}$(film) 3 460, 2 960, 2 140, 1 720, 1 650, 1 430, 1 300, 1 000, 830, 735, and 660 cm^{-1}; δ_H(90 MHz; $CDCl_3$) 1.25 (6 H, s, CMe_2), 1.35—2.05 (5 H, m, CH_2CH_2 and *OH*), 2.90 (2 H, t, *J* 6.5 Hz, $COCH_2$), and 3.85 (d H, s, OCH_3); *m/z* 213 ($M^+ - CH_3$), 200, 185, 170, 150, and 142.

Methyl 2-*Diazo*-5-(2-*hydroxyphenyl*)-3-*oxopentanoate* (**3d**).—A solution of methyl 5-(2-t-butyldimethylsiloxyphenyl)-2-diazo-3-oxopentanoate (**2d**) (600 mg, 1.68 mmol) in acetonitrile (10 ml) was treated with aqueous hydrofluoric acid (40%; 0.52 ml) and stirred at room temperature for 24 h. The mixture was poured into water (50 ml), extracted with ether (2 × 40 ml), dried ($MgSO_4$), and evaporated to give a yellow gum which was chromatographed on silica (light petroleum–ether) to give the *title compound* (**3d**) as a crystalline solid (263 mg, 64%), m.p. 129—131 °C (Found: C, 57.9; H, 4.8; N, 11.25. $C_{12}H_{12}N_2O_4$ requires C, 58.1; H, 4.9; N, 11.30%); $\nu_{max.}$(Nujol) 3 360, 2 160, 1 710, 1 630, 1 600, 1 440, 1 335, 1 200, 1 000, and 755 cm^{-1}; δ_H(90 MHz; $CDCl_3$) 2.85—3.00 (2 H, m, CH_2CO), 3.15—3.30 (2 H, m, CH_2CH_2CO), 3.85 (3 H, s, OCH_3), and 6.75—7.25 (4 H, m, ArH); *m/z* 248 (M^+), 220, and 107.

Methyl 2-*Diazo*-8-*hydroxy*-3-*oxo-octanoate* (**3e**).—A solution of methyl 8-(t-butyldimethylsiloxy)-2-diazo-3-oxo-octanoate (**2e**) (2.50 g, 7.62 mmol) in THF (6 ml) was treated with glacial acetic acid (18 ml) and water (6 ml). The reaction mixture was stirred at room temperature as described above. Similar work-up and chromatography gave the *title compound* (**3e**) as a yellow oil (1.289 g, 79%); $\nu_{max.}$(film) 3 400, 2 950, 2 880, 2 140, 1 720, 1 655, 1 440, 1 320, 1 130, 1 040, 920, and 740 cm^{-1}; δ_H(90 MHz; $CDCl_3$) 1.05—2.15 [7 H, m, $(CH_2)_3CH_2O$ and *OH*], 2.85 (2 H, t, *J* 7.0 Hz, CH_2CO), 3.65 (2 H, t, *J* 6.0 Hz, CH_2O), and 3.80 (3 H, s, OCH_3); *m/z* 215 (MH^+), 186 and 142.

Methyl 2-*Diazo*-10-*hydroxy*-3-*oxodecanoate* (**3f**).—A solution of methyl 10-(t-butyldimethylsiloxy)-3-oxodecanoate (**2f**) (1.00 g, 2.809 mmol) in THF (2.5 ml) was treated with glacial acetic acid (7.5 ml) and water (2.5 ml). The reaction mixture was stirred at room temperature as described above. Similar work-up and chromatography gave the *title compound* (**3f**) as a yellow oil (551 mg, 81%); $\nu_{max.}$(film) 3 400, 2 940, 2 860, 2 140, 1 725, 1 660, 1 440, 1 130, and 745 cm^{-1}; δ_H(90 MHz; $CDCl_3$) 1.20—1.80 [11 H, m, $(CH_2)_5CH_2O$ and *OH*], 2.85 (2 H, t, *J* 7.0 Hz, CH_2CO), 3.65 (2 H, t, *J* 6.5 Hz, CH_2O), and 3.85 (3 H, s, OCH_3); *m/z* 243 (MH^+), 214, 208, 180, 155, and 142.

Cyclisation Reactions

Methyl 3-*Oxo-oxepane*-2-*carboxylate* (**11**).—A suspension of rhodium acetate (7 mg, 0.016 mmol) in refluxing dry benzene (130 ml) was treated dropwise with a solution of methyl 2-diazo-

7-hydroxy-3-oxoheptanoate (**3b**) (800 mg, 4.00 mmol) in benzene (120 ml) under nitrogen. After addition of all the diazo alcohol, the reaction mixture was heated under reflux for a further 0.5 h, allowed to cool, then filtered through a short pad of Celite. The filtrate was evaporated to give a yellow oil which was distilled directly to give the *title compound* (**11**) as a colourless oil (536 mg, 78%), b.p. 80 °C at 0.35 mmHg (Found: C, 55.8; H, 7.1. $C_8H_{12}O_4$ requires C, 55.8; H, 7.0%); $\nu_{max.}$(film) 3 460, 2 960, 2 856, 1 760, 1 720, 1 660, 1 620, 1 450, 1 385, 1 325, 1 275, 1 130, 1 020, 960, and 735 cm^{-1}; δ_H(250 MHz; $CDCl_3$) 1.40—2.10 (4 H, m, $CH_2CH_2CH_2O$, keto/enol), 2.50—2.65 (2 H, m, $COCH_2$, enol), 2.86—3.00 (1 H, m, CHHCO, keto), 3.45—3.58 (2 H, m, CH_2O, keto), 3.80 (3 H, s, OCH_3, keto), 3.83 (3 H, s, OCH_3, enol masking 2 H, t, CH_2, enol), 4.25—4.40 (1 H, m, CHH, keto), 4.50 (1 H, s, $COCHCO_2Me$, keto), and 10.85 (1 H, s, OH, enol); δ_C(62.9 MHz; $CDCl_3$) 22.60, 23.51, 30.65, 31.84, 33.13, 41.59, 51.48, 52.25, 72.86, 73.35, 86.12, 127.55, 166.52, 170.07, and 207.83; *m/z* 172 (M^+), 140, 115, 113, and 55.

Methyl 7,7-Dimethyl-3-oxo-oxepane-2-carboxylate (**12**).—Rhodium acetate (5 mg, 0.0113 mmol) in dry benzene (9 ml) was treated at reflux with methyl 2-diazo-7,7-dimethyl-7-hydroxy-3-oxoheptanoate (**3c**) (57 mg, 0.25 mmol) in benzene (8 ml) under nitrogen as above, followed by a similar work-up and distillation to give the *title compound* (**12**) as a colourless oil (36 mg, 72%), b.p. 70 °C/0.015 mmHg (Found: M^+, 200.1043. $C_{10}H_{16}O_4$ requires *M*, 200.1048); $\nu_{max.}$(film) 3 440, 2 980, 2 960, 2 880, 1 740, 1 650, 1 630, 1 450, 1 325, 1 255, and 1 200 cm^{-1}; δ_H(250 MHz; $CDCl_3$) 1.20 (6 H, ~s, Me_2C, keto), 1.21 (6 H, ~s, Me_2C, enol), 1.55—2.00 (4 H, m, $COCH_2CH_2CH_2$, keto/enol), 2.28—2.40 (2 H, m, CH_2CO, keto), 2.40—2.50 (1 H, m, $COCH_2$, enol), 2.49—3.10 (1 H, m, $COCH_2$, enol), 3.72 and 3.74 (3 H, s, OCH_3), 4.48 (1 H, s, COCHCO, keto), and 11.05 (1 H, s, OH, enol); δ_C(62.9 MHz; $CDCl_3$) 18.95, 18.51, 24.07, 26.48, 29.22, 32.98, 38.92, 39.60, 41.33, 51.52, 52.59, 78.07, 79.62. 121.41, 166.95, 169.54, 171.25, and 208.93; *m/z* 200 (M^+), 185, 129, 111, and 69.

Methyl 3-Oxo-2,3,4,5-tetrahydro-1-benzoxepine-2-carboxylate (**13**).—Rhodium acetate (6 mg, 0.013 mmol) in benzene (22 ml) was treated at reflux with methyl 2-diazo-5-(2-hydroxyphenyl)-3-oxopentanoate (**3d**) (131 mg, 0.528 mmol) in benzene (18 ml) under nitrogen as above, followed by a similar work-up and distillation to give the *title compound* (**13**) as a pale yellow oil (82 mg, 71%), b.p. 104—112 °C/0.07 mmHg (Found: M^+, 220.0744. $C_{12}H_{12}O_4$ requires *M*, 220.0736); $\nu_{max.}$(film) 3 500, 2 960, 2 940, 1 760, 1 730, 1 660, 1 625, 1 615, 1 490, 1 450, 910, and 650 cm^{-1}; δ_H(250 MHz; $CDCl_3$) 2.68—2.80 (2 H, m, CH_2CH_2Ar, keto/enol), 2.98—3.40 (2 H, m, CH_2CH_2CO, keto/enol), 3.85 (3 H, s, OCH_3, keto), 3.90 (3 H, s, OCH_3, enol), 5.00 (1 H, s, CH_2COCH, keto), 7.04—7.22 (4 H, m, ArH, keto/enol), and 11.00 (1 H, s, OH, enol); δ_C(62.9 MHz; $CDCl_3$), 26.68, 27.16, 31.03, 39.86, 51.91, 52.53, 86.35, 116.90, 120.32, 121.64, 121.87, 124.59, 124.84, 127.12, 127.41, 128.08, 128.98, 130.26, 130.52, 156.17, 159.26, 165.36, 165.71, and 204.09; *m/z* 220 (M^+), 188, 161, 149, 91, and 77.

Methyl 3-Oxo-oxecane-2-carboxylate (**14**).—Rhodium acetate (5 mg, 0.011 mmol) in dry benzene (50 ml) was treated at reflux with methyl 2-diazo-8-hydroxy-3-oxo-octanoate (**3e**) (297 mg, 1.38 mmol) in benzene (40 ml) under nitrogen as described above, followed by a similar work-up and chromatography on silica to give the *title compound* (**14**) as a colourless oil (61.8 mg, 24%), b.p. 140—145 °C/0.25 mmHg (Found: M^+, 186.0890. $C_9H_{14}O_4$ requires *M*, 186.0892); $\nu_{max.}$(film) 3 400, 2 940, 2 860, 1 750, 1 720, 1 660, 1 620, 1 440, 1 380, 1 240, 1 065, 1 020, 910, 800, and 730 cm^{-1}; δ_H(250 MHz; $CDCl_3$) 1.50—1.95 [6 H, m, $(CH_2)_3CH_2O$, keto/enol], 2.91—3.06 and 2.37—2.48 (2 H, s m, CH_2CO, keto/enol), 3.78 and 3.80 (3 H, 2 s, OCH_3, keto/enol), 3.62—4.10 (2 H, m, CH_2CO, keto/enol), 4.15 (1 H, s, COCHCO, keto), and 10.90 (1 H, s, OH, enol); δ_C(62.9 MHz; $CDCl_3$) 22.10, 24.99, 25.18, 25.49, 28.87, 30.69, 32.03, 38.01, 51.25, 52.54, 72.88, 73.70, 84.82, 120.94, 166.40, 169.60, 170.71, and 211.93; *m/z* 286 (M^+), 154, 129, 126, 97, and 55.

Preparation of Derivatives

Methyl 3-(t-Butyldimethylsiloxy)-4,5,6,7-tetrahydro-oxepine-2-carboxylate (**16**).—A solution of methyl 3-oxo-oxepane-2-carboxylate (**11**) (150 mg, 0.827 mmol) in dry diethyl ether (6.5 mg) was treated at room temperature with triethylamine (0.17 ml, 123 mg, 1.22 mmol), followed by the dropwise addition of t-butyldimethylsilyl trifluoromethanesulphonate (0.30 ml, 346 mg, 1.308 mmol). After 1.5 h the reaction mixture was poured into water (30 ml), extracted with ether (50 ml), and the extract washed with saturated aqueous sodium hydrogen carbonate (10 ml) and then water (3 × 20 ml) until neutral, dried ($MgSO_4$), and evaporated to give the crude product as a yellow-brown oil (290 mg). The crude product was chromatographed on silica (light petroleum–ether) and subsequently distilled to give the *title compound* (**16**) as a colourless oil (206 mg, 83%), b.p. 135—140 °C/0.35 mmHg (Found: C, 58.9; H, 9.2. $C_{14}H_{26}O_4Si$ requires C, 58.7; H, 9.15%); $\nu_{max.}$(film) 2 950, 2 860, 1 720, 1 620, 1 435, 1 370, 1 240, 1 210, 1 155, 1 060, 885, 780, and 735 cm^{-1}; δ_H(250 MHz; $CDCl_3$) 0.15 (6 H, s, Me_2Si), 0.92 (9 H, s, Bu^{t}Si), 1.53—1.62 (2 H, m, CH_2CH_2O), 1.78—1.90 (2 H, m, $CH_2CH_2CH_2O$), 2.43—2.55 (2 H, m, $CH_2C{=}C$), 3.70 (3 H, s, OCH_3), and 3.82 (2 H, t, *J* 5.0 Hz, CH_2O); δ_C(62.9 MHz; $CDCl_3$) −4.15 (2 carbons) 18.8, 22.50, 25.61 (3 carbons), 31.59, 35.99, 50.82, 72.88, 135.58, 160.07, and 164.19; *m/z* 271 (M^+ − CH_3), 255, 229, 89, 73, and 59.

Methyl 3-(t-Butyldimethylsiloxy)-4,5,6,7-tetrahydro-oxecine-2-carboxylate (**17**).—A solution of methyl 3-oxo-oxecane-2-carboxylate (**14**) (117 mg, 0.629 mmol) in dry diethyl ether (5.0 ml) was treated at room temperature with triethylamine (0.12 ml, 88.88 mg, 0.88 mmol) followed by the dropwise addition of t-butyldimethylsilyl trifluoromethanesulphonate (0.22 ml, 24.93 mg, 0.943 mmol), as described above. Similar work-up, chromatography, and distillation gave the *title compound* (**17**) as a colourless oil (81 mg, 39%), b.p. 135 °C at 0.25 mmHg (Found: M^+, 243.1047. $C_{15}H_{28}O_4Si - C_4H_9$ requires 243.1053); $\nu_{max.}$(film) 2 960, 2 940, 2 860, 1 720, 1 620, 1 445, 1 370, 1 315, 1 230, 1 150, 1 065, 840, and 785 cm^{-1}; δ_H(250 MHz; $CDCl_3$) 0.20 (6 H, s, Me_2Si), 0.96 (9 H, s, Bu^{t}Si), 1.58—1.83 [6 H, m, $(CH_2)_3CH_2O$], 2.40—2.49 (2 H, m, $CH_2C{=}C$), 3.73 (3 H, s, OCH_3), and 3.87—3.97 (2 H, m, CH_2O); δ_C(62.9 MHz; $CDCl_3$) − 3.74 (2 carbons), 18.42, 25.76, 25.80 (3 carbons), 27.34, 27.53, 33.57, 50.73, 73.75, 128.82, 160.65, and 163.81; *m/z* 243 (M^+ − C_4H_9).

Methyl 3-Benzylamino-4,5,6,7-tetrahydro-oxepine-2-carboxylate (**18**).—A stirred solution of methyl 3-oxo-oxepane-2-carboxylate (**11**) (150 mg, 0.872 mmol) in dichloromethane (2.0 ml) was treated with benzylamine (0.105 ml, 103 mg, 0.96 mmol) under nitrogen at room temperature for 48 h. The mixture was then evaporated and the residue chromatographed on silica (light petroleum–ether). The crude product decomposed on purification to give starting material (**11**) as a pale yellow oil (53 mg, 23%) and the *title compound* (**18**) as a crystalline solid (32 mg, 14%), m.p. 115—117 °C (Found: C, 68.7; H, 7.4; N, 5.4. $C_{15}H_{19}NO_3$ requires C, 68.9; H, 7.3; N, 5.4%); $\nu_{max.}$(Nujol) 3 300, 1 640, 1 600, 1 495, 1 435, 1 425, 1 255, 1 060, 775, and 740 cm^{-1}; δ_H(250 MHz; $CDCl_3$) 1.40—1.53 (2 H, m, CH_2CH_2O), 1.76—1.88 (2 H, m, $CH_2CH_2CH_2O$), 2.53—2.64 (2 H, m,

$CH_2C{\equiv}C$), 3.75 (3 H, s, OCH_3), 3.77 (2 H, t, *J* 6.5 Hz, CH_2O), 4.43 (2 H, d, *J* 6.5 Hz, CH_2NH_2), 7.21—7.38 (5 H, m, ArH), and 8.33—8.56 (1 H, br s, NH); *m/z* 261 (M^+), 202, 174, and 91.

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